Focal, High Dose, and Fractionated Modified Stereotactic Radiation Therapy for Lung Carcinoma Patients

A Preliminary Experience

Minoru Uematsu, M.D.[1]
Akira Shioda, R.T.T.[1]
Kazuhiko Tahara, R.T.T.[1]
Toshiharu Fukui, R.T.T.[1]
Fuyumi Yamamoto, M.D.[1]
Gentaro Tsumatori, M.D.[2]
Yuichi Ozeki, M.D.[2]
Teruhiro Aoki, M.D.[2]
Masazumi Watanabe, M.D.[2]
Shoichi Kusano, M.D.[1]

[1] Division of Radiation Oncology, National Defense Medical College, Tokorozawa, Saitama, Japan.

[2] Division of Thoracic Surgery, National Defense Medical College, Tokorozawa, Saitama, Japan.

Presented in part at the 38th Annual Meeting of the American Society for Therapeutic Radiology and Oncology, Los Angeles, California, October 1996, and the Third Congress of the International Stereotactic Radiosurgery Society, Madrid, Spain, June 1997.

Supported in part by grants from the Japanese Society for Therapeutic Radiology and Oncology and from the Ministry of Health and Welfare of Japan.

Address for reprints: Minoru Uematsu, M.D., Division of Radiation Oncology, National Defense Medical College, 3-2, Namiki, Tokorozawa, Saitama, 359, Japan.

Received May 28, 1997; revision received September 19, 1997; accepted September 19, 1997.

BACKGROUND. Stereotactic radiation therapy is highly effective in the treatment of small brain metastases, regardless of the histology. This suggests that small extracranial malignancies may be curable with similar radiation therapy. The authors developed a novel treatment unit for administering such therapy.

METHODS. The unit consisted of a linear accelerator (linac), an X-ray simulator (X-S), computed tomography (CT), and a table. The gantry axes of the three machines were coaxial and could be matched by rotating the table. Patients were instructed to perform shallow respiration with oxygen. The motion of the tumor was monitored with the X-S. When the motion was slight enough, the table was rotated to the CT. To include all geometric movement on the CT images, each scan was made while the patient was performing shallow respiration. After the CT positioning, the table was rotated to the linac, and non-coplanar treatment was given. Beginning in October 1994, 45 patients with 23 primary or 43 metastatic lung carcinomas were treated. Radiation doses at the 80% isodose line were 30–75 gray in 5–15 fractions over 1–3 weeks with or without conventional radiation therapy.

RESULTS. The treatment was performed with no or minimal adverse acute symptoms. The daily treatment time was short. During a median follow-up of 11 months, local progression occurred in 2 of 66 lesions. Interstitial changes in the lung were limited.

CONCLUSIONS. With this unit and procedure, focal radiation therapy similar to stereotactic radiation therapy is possible for extracranial sites. The preliminary experience appeared safe and promising, and further exploration of this approach is warranted. *Cancer* **1998;82:1062–70.** © *1998 American Cancer Society.*

KEYWORDS: radiation therapy, treatment unit, lung carcinoma, stereotactic, high dose, focal, fractionated, extracranial.

Stereotactic radiation therapy (SRT) and stereotactic radiosurgery (SRS) have been shown to be highly effective for treating small and well-circumscribed brain metastases, regardless of the primary site or histology.[1–3] This suggests that small and well-circumscribed extracranial malignancies may be controlled with similar focal, high dose radiation therapy. However, it is not easy to administer such highly accurate treatment to extracranial sites, because the lesions are movable even after the bony structures are fixed. To overcome the difficulties in targeting and localization of the lesions, we developed a novel treatment unit to achieve direct positioning of a moving target with a computed tomography (CT) scanner and immediate radiation therapy with a linear accelerator (linac). The key concept of this treat-

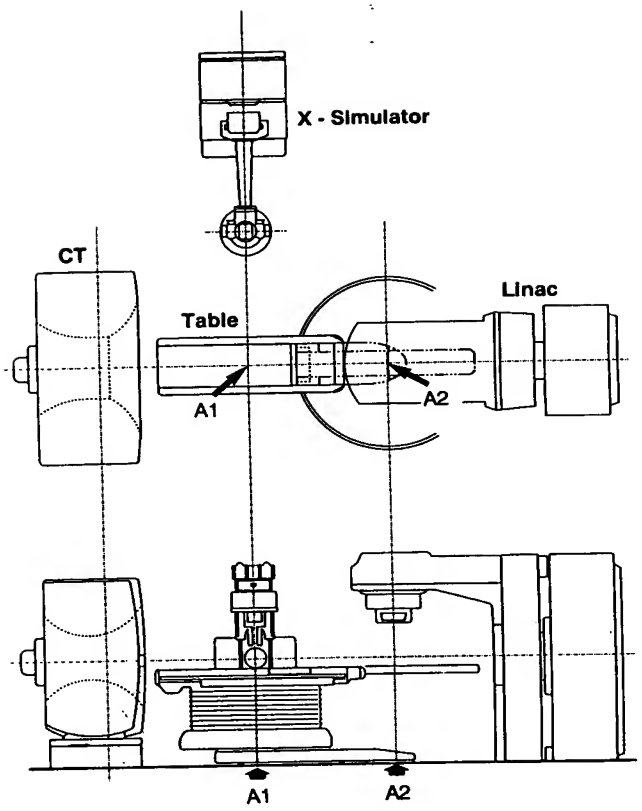


FIGURE 1. A diagram of the fusion of CT and linac (FOCAL) unit is shown. The gantry axis of the linac is coaxial with that of computed tomography (CT) and the X-ray simulator (X-S). The table has two rotation axes: A1 is for rotation between the three machines, and A2 is for isocentric rotation to make non-coplanar treatment arcs.

ment approach is a fusion of CT and linac (FOCAL). In this report, we present the methodology of the FOCAL unit and our preliminary experience with treating primary and metastatic lung carcinomas.

MATERIALS AND METHODS

The FOCAL unit is composed of a linac, an X-ray simulator (X-S), a CT, and a treatment table (Fig. 1), and a new version of our previously reported dual CT-linac unit for SRT of intracranial lesions without a cranially fixated stereotactic frame.[4,5] The gantry axis of the linac is coaxial with that of the X-S and CT. Each gantry axis can be matched, simply by rotating the table around the A1 axis. To make multiple non-coplanar treatment arcs, the table is rotated around the A2 axis. Although, with the old version, patients do not have to move on the table during the positioning and treatment, there should be nonnegligible motions in extracranial sites, mainly with respiration. Thus, the X-S is added to monitor the motion of the extracranial tumor and to check whether or not its motion is acceptably slight. Because of the clear visibility with the X-S and CT, lung carcinomas are chosen as one of the main targets of this treatment.

For clinical use, patients who can maintain a supine position and calm respiration can be candidates for this treatment. We ensure that all candidates are well informed about the concept, methodology, and various possibilities of this new and experimental treatment. All patients are instructed to perform shallow and fairly rapid respiration on the treatment table. An oxygen (3000–7000 cc/minute) mask is always used to help patients maintain shallow respiration during the positioning and treatment. Abdominal belts are sometimes added to minimize the motion further. Initially, with the shallow respiration, the position of the tumor is monitored with the X-S and its motion is evaluated. The size of the craniocaudal motion of the tumor is classified into three categories: minimal or negligible (less than or equal to 0.5 cm), small enough (greater than 0.5 cm but less than or equal to 1 cm), or not small (greater than 1 cm). When the tumor is spherical and its motion is minimal or negligible, treatment similar to SRT for intracranial lesions is possible with multiple non-coplanar arcs using a single isocenter (Fig. 2A). When the tumor is nearly spherical and/or its motion is slight enough, the similar treatment is possible, although more normal tissues are included within the high dose area (Fig. 2B). When the tumor is different from a spherical shape or its motion is not slight we usually abandon the treatment but sometimes try to treat using a two-isocenter technique (Fig. 2C). These multiple non-coplanar arc treatments are better with regard to dose distribution than the conventional radiation therapy (Figs. 2D and 2E).

After the X-S monitoring, if the motion is acceptable (Fig. 3A), the table is rotated to the CT and serial scans are performed with 2–5 mm slice thickness and interval, depending on the target size (Fig. 3B). To include all geometric movement of the tumor within the CT images, each scan is slowly performed (4 seconds/slice) against the shallow and fairly rapid respiration. The CT window width is large (+1000 to +2000 HU) and the CT window level (−500 to −1000 HU) is low, to include the movement of the lung tumor and its partial volume effects within the CT images. Using the CT images, the target volume is planned and the center of the target volume is determined (Fig. 3C). For most Japanese patients, it is easy to match the center of the target volume with the horizontal plane of the gantry axis of the CT, because the thickness of the body is thin enough to position within the CT gantry. However, it is often impossible to do this for

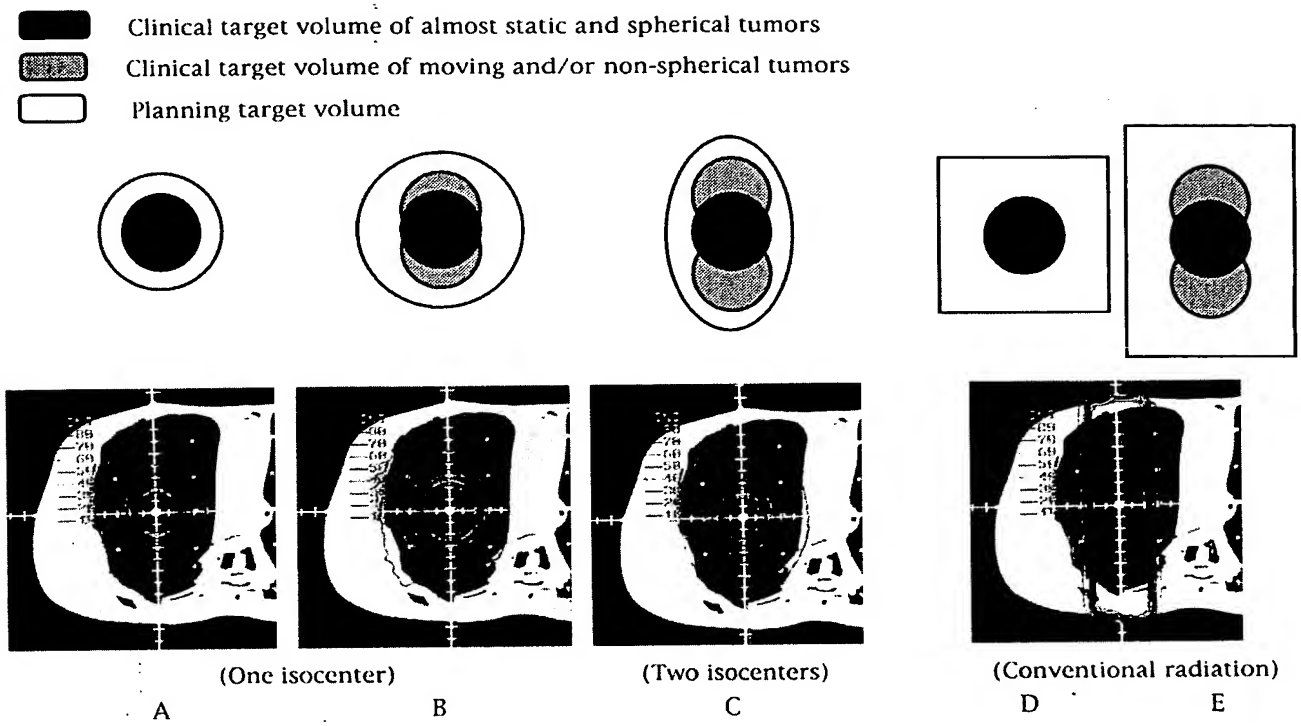


FIGURE 2. A schematic relationship is shown between the clinical and planning target volume in the anterior-posterior view with the dose distribution in the central axial plane (10%, 20%, 30%, 40%, 50%, 60%, 70%, and 80% isodose lines are shown). The size of the static and spherical tumor is 2 cm in diameter. Its cranio-caudal motion is 0 cm in A and D, 1 cm in B, and 2 cm in C and E. The field margin between the clinical and planning target volume is 0.5 cm (1 cm in diameter) in A, B, and C with the fusion of CT and linac (FOCAL) method, and 1 cm in D and E with the conventional method. The calculated volumes of the 80% and 50% isodose lines are 14 cc and 16 cc in A, 33 cc and 39 cc in B, and 28 cc and 32 cc in C. With two anterior-posterior portals, the volumes of the 80% and 50% isodose lines are about 290 cc in D and 430 cc in E. With four portals, the volume of the 80% isodose line is reduced to about 65 cc in D and 95 cc in E; however, that of 50% is increased to about 500 cc in D and 750 cc in E.

the vertical plane, because the size of the CT is not large enough for the width of the body. In such instances, a tiny metallic ball, which is clearly visible on CT, is put on the anterior surface of the body as a vertical marker (Fig. 3C).

After the CT positioning, the table is rotated to the linac. Already, at least, the center of the target volume is matched with the horizontal plane of the gantry axis of the linac by the CT process. To match the center of the target volume with the vertical plane of the gantry axis of the linac, the table position is adjusted horizontally until the vertical laser pointer of the linac is aligned with the tiny metallic ball as a vertical marker. Immediately after this process, radiation therapy is given, usually with multiple non-coplanar arcs using a circular aperture. To make daily management time short, radiation dosimetry is usually performed before the treatment day. On each treatment day, patients receive only one or two of the planned treatment arcs just after the X-S monitoring and CT positioning described above.

Between October 1994 and February 1997, more than 110 lesions were treated with this unit. Of these, 66 lesions in 45 patients were primary or metastatic lung carcinomas and constituted the clinical material of this study. Clinical use of this experimental treatment was accepted by the institutional ethical committee, and informed consent was obtained from all patients. All patients were medically inoperable or refused surgery. There were 27 male and 18 female patients. Ages ranged from 28 to 86 years, with a median age of 65 years. Twenty-three of the 66 lesions were primary nonsmall cell lung carcinomas (5 squamous cell carcinomas, 17 adenocarcinomas, 1 not specified). The remainder were metastatic cancers, and their primary sites were colon-rectum (15 lesions), lung (11), breast (8), kidney (3), soft tissue (3), or others (3). The sizes of the tumors ranged from 0.8 to 4.8 cm on CT, with a median of 2.5 cm. The largest size of the tumor was initially up to 3 cm, but recently up to 5 cm, provided that the target volume could be included within the 80% isodose line (Tables 1 and 2). There were three

TABLE 1
Summary of Primary Lung Carcinomas Treated with the FOCAL Unit

No.	Stage	Histology	Geometric motion (cm)	Tumor size on CT (cm)	FOCAL RT PTV (cm), (Gy/Fr/wks)	Conventional RT area, (Gy/Fr/wks)	Local control	Status, mos
1	T1N0M0	Squamous	0.5	2.5 (1.5)[a]	2.1, 40/10/2	L-R, 45/25/5	Yes	A&W, 31
2	T2N0M0	Squamous	0.5	4 (2)[a]	2.1, 30/6/1	L-R, 60/33/7	Yes	A&W, 30
3	T1N0M0	Adenoca	<0.5	2	3.1, 60/15/3	None	Yes	A&W, 24
4	T2N0M0	Adenoca	0.5	3	4.1, 60/10/2.5	None	Yes	A&W, 20
5	T1N0M0	Adenoca	0.5	1.5	3.1, 60/10/2	None	Yes	A&W, 20
6	T2N0M0	Adenoca	1	3.1	4.8, 65/13/3	None	Yes	A&W, 20
7	T1N0M0	NSCLC	<0.5	1.8	3.1, 60/10/2	None	Yes	A&W, 18
8	T2N0M0	Adenoca	1.3	4	2.8, 60/10/2[b]	None	Yes	A&W, 18
9	T3N0M1	Adenoca	0.5	4.8	2.8, 60/10/2[b] 4.5, 50/10/2[b] 3.1, 50/10/2[b]	None	No	AwD, 12
10	T2N0M0	Adenoca	1	3.5	5.1, 70/15/3	None	Yes	A&W, 12
11	T2N0M0	Adenoca	<0.5	4.5 (3.5)[a]	5.1, 40/8/2	L, 50/25/5.5	Yes	A&W, 12
12	T2N0M0	Adenoca	<0.5	3.5	5.1, 66/11/2.5	None	Yes	A&W, 12
13	T3N0M0	Squamous	<0.5	2	3.5, 50/10/2.5	None	Yes	ICD, 12
14	T3N0M0	Adenoca	<0.5	4 (3)[a]	4.6, 45/11/2.5	L, 50/25/6	Yes	A&W, 9
15	T1N0M0	Adenoca	1	2.2	4.1, 60/10/2	None	Yes	A&W, 9
16	T2N0M0	Squamous	<0.5	4.2	5.1, 66/12/3[b] 3.1, 66/12/3[b]	None	Yes	A&W, 9
17	T2N0M0	Squamous	<0.5	4 (3)[a]	3.5, 40/8/2	L, 50/25/5.5	Yes	A&W, 6
18	T1N0M0	Adenoca	0.5	2.6	4.1, 54/9/2	None	Yes	A&W, 6
19	T1N0M0	Squamous	0	1.5	3.5, 50/10/2	None	Yes	A&W, 6
20	T1N0M0	Adenoca	<0.5	2.5 (2.2)[a]	4.1, 32/4/1	L, 50/25/6.5	Yes	A&W, 9
21	T2N0M0	Adenoca	<0.5	4.5 (4)[a]	5.1, 40/4/1	L, 50/25/5	Yes	AwD, 9
22	T2N0M0	Adenoca	<0.5	3.5	5.1, 60/5/1	None	Yes	A&W, 6
23	T1N0M0	Adenoca	0.5	2.1	4.1, 48/4/1	None	Yes	A&W, 6

FOCAL: fusion of CT and linac; Squamous: squamous cell carcinoma; Adenoca: adenocarcinoma; NSCLC: nonsmall cell lung carcinoma; L: local; L-R: local and regional; PTV: planning target volume; A&W: alive and well; AwD: alive with disease; ICD: intercurrent death; RT: radiation therapy; CT: computed tomography; Fr: fractions.

[a] Size after conventional treatment.

[b] Two-isocenter treatment.

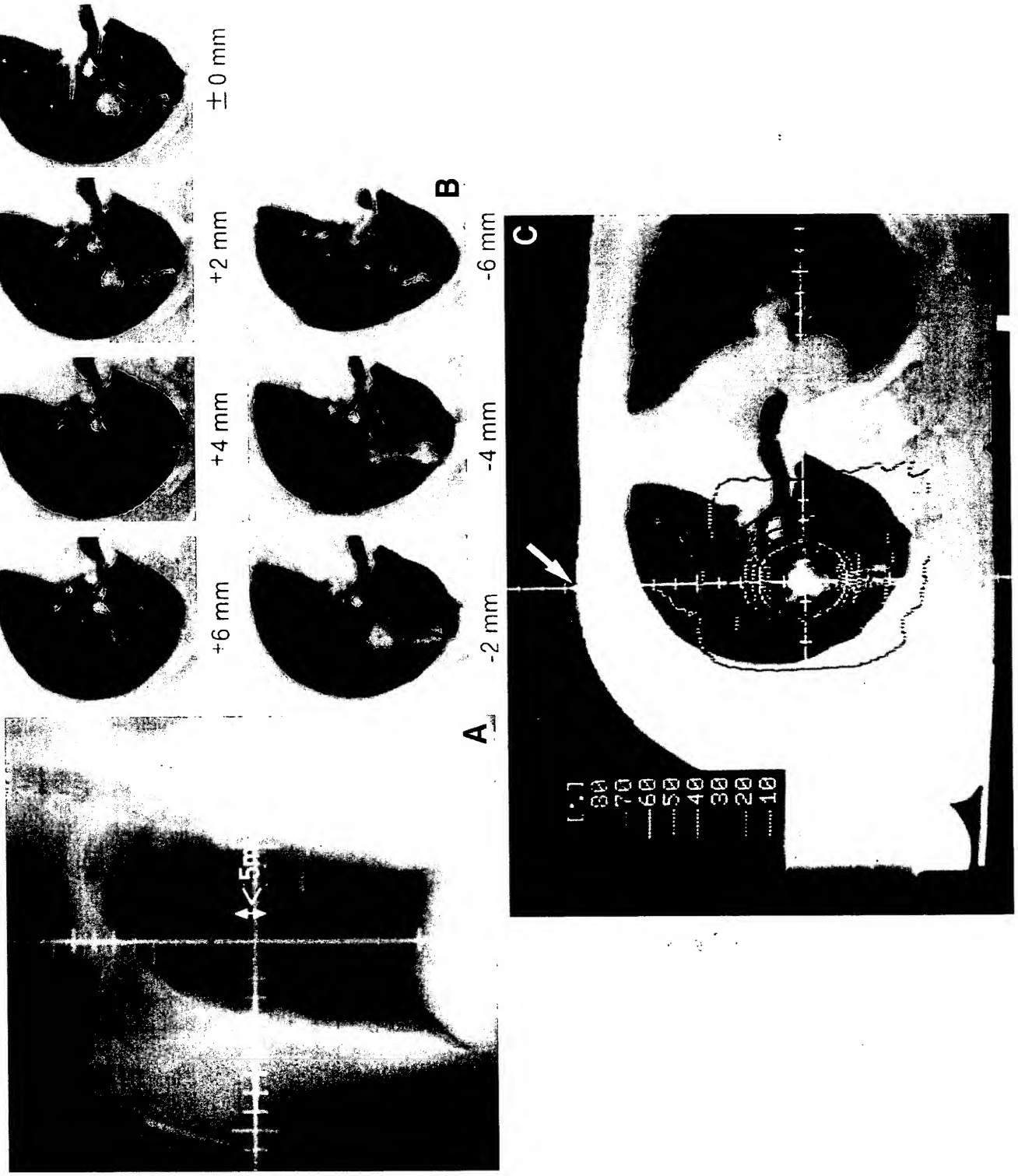
patients who were unable to receive this treatment because of excessive respiratory motions.

Radiation doses at the 80% isodose line were 30–75 Gy given in 5–15 fractions over 1–3 weeks, with 6–15 non-coplanar arcs. The 80% isodose line was planned to include the clinical target volume on the serial CT, usually with additional margins 1–2 cm in diameter. Just before this focal high dose treatment, 7 of the 23 patients with primary nonsmall cell lung carcinoma also received conventional radiation therapy of 45–60 Gy given in 25–33 fractions over 5–7 weeks. In five of the seven patients, the conventional radiation fields were only local without regional lymph node sites, because their tumors had invasive and irregular margins (such as pleural indentations) and seemed to be at high risk for marginal recurrence only with focal radiation therapy. The remaining two patients received local and regional lymph node irradiation, according to the recommendations of their referring physicians (Table 1).

In seven patients whose respiratory motion was small enough but somewhat irregular during the X-S monitoring, to check whether or not the tumor had unexpected motion after CT positioning, the table was rerotated to the CT and rescanning was performed after the daily irradiation. In 10 patients, including the first 5, blood gases were monitored before, during, and after treatment for several weeks. Patients were followed with CT scans until May 1997 or the time of death. Follow-up times ranged from 3 to 31 months, with a median of 11 months. Treatment results in this preliminary study were judged according to whether or not local control was achieved. When the tumor did not show local progression on follow-up CT, local control was judged to have been achieved. There were three other patients who were unable to receive this treatment, because of excessive motion of the tumor.

RESULTS

The planned treatment was safely performed on all 45 patients with no or minimal adverse acute symptoms.


±0 mm
+2 mm
+4 mm
+6 mm
B
-6 mm
-4 mm
-2 mm
A
C
5m
[.]
60
70
60
50
40
30
20
10

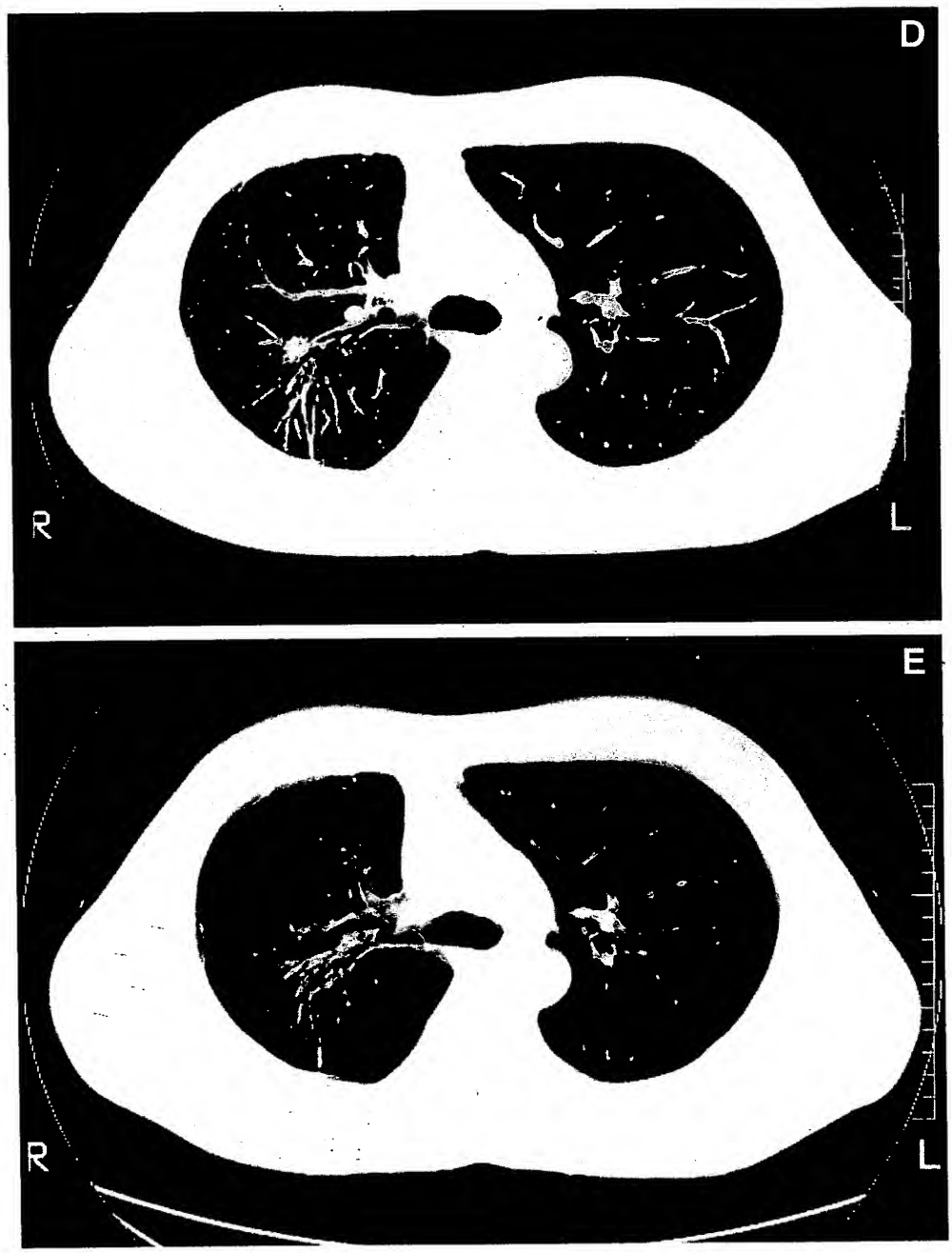


FIGURE 3. Local recurrence of primary T1N0M0 adenocarcinoma of the lung (1 year after limited surgery) is represented. (A) With the oxygen, the patient maintains shallow respiration. The extent of the craniocaudal motion of the tumor is less than 5 mm on the X-ray simulator monitoring. (B) Serial computed tomography scans detect the moving tumor. All scans are performed with shallow respiration. (Abnormal linear densities visible between the tumor and the posterior chest wall are judged to be surgical scars.) (C) The center of the target volume is determined and isodose lines are presented. A tiny metallic ball is placed on the anterior surface of the body (arrow). (D and E) A treated area is shown 1 and 22 months after the focal, high dose, and fractionated radiation therapy. The clinical course is promising.

TABLE 2
Summary of Metastatic Lung Carcinomas Treated with the Focal Unit

No.	Primary site	Histology	Geometric motion (cm)	Tumor size on CT (cm)	FOCAL RT PTV (cm), (Gy/Fr/wks)	Local control	Status, mos
1	Breast	Adenoca	<0.5	1	2.8, 50/10/2	Yes	A&W, 24
2	Soft tissue	MFH	<0.5	3	4.1, 60/12/2.5	Yes	DoD, 21
3	Soft tissue	MFH	<0.5	1	2.1, 60/12/2.5	Yes	DoD, 21
4	Colon	Adenoca	<0.5	2.5	2.4, 76/8/6	No	DoD, 20
5	Thymus	Thymoma	1	2.5	3.5, 40/10/2	Yes	AwD, 20
6	Lung	Adenoca	<0.5	1.2	2.4, 56/8/2	Yes	A&W, 20
7	Lung	Adenoca	0.5	2	3.1, 56/8/2	Yes	A&W, 20
8	Lung	Adenoca	1	1.5	3.1, 56/8/2	Yes	A&W, 20
9	Lung	Adenoca	1	1.5	3.1, 56/8/2	Yes	A&W, 20
10	Soft tissue	MFH	<0.5	2	3.1, 50/10/2	Yes	DoD, 16
11	Kidney	RCC	0.5	2.1	3.1, 51/7/1.5	Yes	AwD, 13
12	Kidney	RCC	0.5	3	4.1, 60/10/2	Yes	AwD, 13
13	Kidney	RCC	1	2.8	4.1, 60/10/2	Yes	AwD, 13
14	Breast	Adenoca	<0.5	2.1	3.5, 50/10/2	Yes	AwD, 11
15	Breast	Adenoca	<0.5	1	2.4, 50/10/2	Yes	AwD, 11
16	Rectum	Adenoca	<0.5	3.4	4.6, 65/13/3	Yes	AwD, 11
17	Rectum	Adenoca	<0.5	2.9	4.6, 65/13/3	Yes	AwD, 11
18	Breast	Adenoca	1	3	4.6, 60/15/3	Yes	AwD, 11
19	Rectum	Adenoca	<0.5	2.9	4.1, 60/12/3	Yes	AwD, 10
20	Rectum	Adenoca	0.5	2.6	4.1, 60/12/3	Yes	AwD, 10
21	Breast	Adenoca	1	1.6	3.1, 60/10/2	Yes	AwD, 9
22	Lung	Adenoca	1	4	5.1, 50/10/2	Yes	DoD, 9
23	Rectum	Adenoca	0.5	1.8	2.8, 33/6/1	Yes	DoD, 8
24	Colon	Adenoca	1	2.8	4.1, 50/5/1	Yes	A&W, 7
25	Colon	Adenoca	1	2	3.5, 50/5/1	Yes	A&W, 7
26	Breast	Adenoca	<0.5	2.1	3.1, 48/6/1	Yes	DoD, 7
27	Colon	Adenoca	1	2	3.5, 60/10/2	Yes	A&W, 6
28	Breast	Adenoca	0.5	1.2	3.1, 50/10/2	Yes	AwD, 6
29	Breast	Adenoca	0.5	1.2	3.1, 50/10/2	Yes	AwD, 6
30	Breast	Adenoca	0.5	1.8	3.5, 50/10/2	Yes	AwD, 6
31	Lung	Squamous	<0.5	2.5	3.5, 55/11/2	Yes	ICD, 6
32	Rectum	Adenoca	0.5	1	2.5, 54/9/2	Yes	AwD, 6
33	Rectum	Adenoca	0.5	1	2.5, 54/9/2	Yes	AwD, 6
34	Lung	Adenoca	<0.5	2.5	3.1, 65/13/3	Yes	DoD, 6
35	Lung	Adenoca	<0.5	2.5	3.1, 65/13/3	Yes	DoD, 6
36	Lung	Adenoca	<0.5	2.5	3.1, 65/13/3	Yes	DoD, 6
37	Colon	Adenoca	0.5	1	2.8, 50/5/1	Yes	A&W, 5
38	Colon	Adenoca	1	2	3.1, 50/5/1	Yes	A&W, 5
39	Ovary	Clear cell	1	4	5.1, 50/10/2	Yes	DoD, 4
40	Rectum	Adenoca	0.5	1.5	3.1, 50/5/1	Yes	AwD, 4
41	Rectum	Adenoca	0.5	1.8	3.5, 50/5/1	Yes	AwD, 4
42	Liver	HCC	<0.5	2.2	3.5, 40/5/1	Yes	DoD, 3
43	Lung	Pulmonary blastoma	<0.5	1.7	3.5, 50/10/3	Yes	DoD, 3

FOCAL: fusion of CT and linac; Adenoca: adenocarcinoma; MFH: malignant fibrous histiocytosis; RCC: renal cell carcinoma; Clear cell: clear cell carcinoma; HCC: hepatocellular carcinoma; PTV: planning target volume; CT: computed tomography; RT: radiation therapy; Fr: fractions; A&W: alive and well; AwD: alive with disease; DoD: Dead of disease.

Only 1 patient reported mild appetite loss during the treatment period, and 4 had transient dry cough 1–3 months after the treatment. In seven patients with shallow but somewhat irregular respiration, the CT rescanning after the daily treatment showed good reproducibility. The geometric errors on the re-CT images were always less than 0.5 cm. Blood gases were unaffected in all patients who were checked. Interstitial changes in the irradiated lungs were less prominent with this focal, high dose radiation therapy. In most patients treated without conventional radiation therapy, their interstitial changes were minimal or limited (Figs. 3D and 3E). All 66 lesions responded to the treatment, but only 2 of them showed local progres-

sion thereafter on follow-up CT. Thus, the crude local progression rate was 3% (2 of 66 lesions). As of May 1997, 34 patients were alive and 11 had died. All deaths were due to systemic metastases or intercurrent disease, not local progression at the treated sites. The daily treatment time with this approach was short enough—about 30 minutes on the first treatment day and about 20 minutes on subsequent days for a single isocenter treatment, including the X-S monitoring, CT positioning, and irradiation.

DISCUSSION

The results of treating lung carcinomas with conventional radiation therapy are not optimal, and local failures are still common even in patients with small tumors.[6–8] In such instances, it is desirable to increase radiation doses to the tumor without increasing the damage to the adjacent normal tissue. This feat is very difficult with conventional radiation therapy; and new approaches, such as three-dimensional conformal radiation therapy (3DCRT), have recently been tried in the treatment of lung carcinoma.[9–11] On the other hand, SRS or SRT, which are the simple variations of 3DCRT, have already made this feat possible in the treatment of intracranial small lesions. The treatment results of small brain metastases are excellent, including those from lung carcinomas.[1–3] In general, SRT seems to be better than SRS for treating malignant tumors because of fractionation.[12–14] Thus, focal, high dose, and fractionated radiation therapy such as SRT seems to be a reasonable approach for treating small lung tumors. Recently, several authors have reported approaches to treating extracranial lesions that have involved modifications of SRS or SRT.[15–17] Lax et al. and Blomgren et al. reported their SRT methods and experiences, mainly with abdominal tumors; they noted good progression free rates.[15,16] Hamilton and Lulu presented their prototype device for the localization of extracranial sites.[17] The FOCAL unit presented here was also developed to achieve the same goal of focal radiation therapy of frameless SRT for extracranial tumors.

Small primary or metastatic lung carcinomas may be potentially good targets for SRT, because the shape is usually nearly spherical; moreover, limited volumes of radiation damage to the lung are not likely to cause severe adverse symptoms compared with those in the brain, in which SRS or SRT have been shown to be safe. Possibly, the largest problem with using SRT to treat small lung carcinomas is the respiratory motion, which may cause positioning error. To overcome this problem, we used an oxygen mask; instructed patients to maintain shallow respiration; monitored patients daily with the X-S; performed direct CT positioning with shallow respiration daily; and administered immediate irradiation, usually with margins less than 2 cm in diameter. So far, the focal high dose treatment with frameless SRT has been performed safely with a good local control rate, although for patients treated thus far the follow-up period was short. The daily management time was short enough for routine clinical use. Total radiation doses, daily fraction sizes, or fractionation schedules presented in this study were all experimental and should be evaluated and optimized in follow-up studies. However, judging from the preliminary experience described in this report, the treatment seems to be safe and promising, and further exploration of this approach is warranted.

REFERENCES

1. Alexander E III, Moriarty TM, Davis RB, Wen PY, Fine HA, Black PM, et al. Stereotactic radiosurgery for the definitive, noninvasive treatment of brain metastases. *J Natl Cancer Inst* 1995;87:34–40.
2. Flickinger JC, Kondoziolka D, Lunsford LD, Coffey RJ, Goodman ML, Shaw EG, et al. A multi-institutional experience with stereotactic radiosurgery for solitary brain metastasis. *Int J Radiat Oncol Biol Phys* 1994;28:797–802.
3. Engenhart R, Kimmig B, Hover K, Wowra B, Romahn J, Lorenz WJ, et al. Long-term follow-up for brain metastases treated by percutaneous single high dose radiation. *Cancer* 1993;71:1353–61.
4. Uematsu M, Fukui T, Shioda A, Tokumitsu H, Takai K, Kojima T, et al. A dual computed tomography linear accelerator unit for stereotactic radiation therapy: a new approach without cranially fixated stereotactic frame. *Int J Radiat Oncol Biol Phys* 1996;35:587–92.
5. Uematsu M, Fukui T, Shioda A, Tokumitsu H, Takai K, Kojima T, et al. Linear accelerator based multifunctional treatment unit for stereotactic radiation therapy for extracranial tumors. *Int J Radiat Oncol Biol Phys* 1995;32(Suppl 1):168.
6. Coy P, Kennelly GM. The role of curative radiotherapy in the treatment of lung cancer. *Cancer* 1980;45:698–702.
7. Kaskowitz L, Graham MV, Emami B, Halverson KJ, Rush C. Radiation therapy alone for stage I non-small cell lung cancer. *Int J Radiat Oncol Biol Phys* 1993;27:517–23.
8. Dosoretz DE, Katin MJ, Blitzer PH, Rubinstein JH, Galmarini DH, Garton GR, et al. Medically inoperable lung carcinoma: the role of radiotherapy. *Semin Radiat Oncol* 1996;6:98–104.
9. Armstrong JG, Burman C, Leibel SA, Fontenla D, Kutcher G, Zelefsky M, et al. Three dimensional conformal radiation therapy may improve the therapeutic ratio of high dose radiation therapy for lung cancer. *Int J Radiat Oncol Biol Phys* 1993;26:685–9.
10. Robertson JM, Turrisi AT, Hazuka MB, Martel MK, Ten Haken RK, Littles FJ, et al. Dose escalation for non-small cell lung cancer using conformal radiation therapy. *Int J Radiat Oncol Biol Phys* 1995;32(Suppl 1):197.
11. Emami B. Three-dimensional conformal radiation therapy in bronchogenic carcinoma. *Semin Radiat Oncol* 1996;6:92–7.
12. Hall EJ, Brenner DJ. The radiobiology of radiosurgery: rationale for different treatment regimens for AVMs and malignancies. *Int J Radiat Oncol Biol Phys* 1993;25:381–5.
13. Larson DA, Flickinger JC, Loeffler JS. The radiobiology of radiosurgery. *Int J Radiat Oncol Biol Phys* 1993;25:557–62.

14. Loeffler JS, Alexander E III, Kooy HM. Stereotactic radiotherapy: rationale, technique, and early results. In: DeSalles AAF, Goetsch SJ. Stereotactic surgery and radiosurgery. Madison, WI: Medical Physics Publishing, 1993:307–20.
15. Lax I, Blomgren H, Naslund I, Svanstrom R. Stereotactic radiotherapy of malignancies in the abdomen: methodological aspects. *Acta Oncol* 1994;33:677–83.
16. Blomgren H, Lax I, Naslund I, Svanstrom R. Stereotactic high dose fraction radiation therapy of extracranial tumors using an accelerator: clinical experience of the first thirty-one patients. *Acta Oncol* 1995;34:861–70.
17. Hamilton AJ, Lulu BA. A prototype device for linear accelerator based extracranial radiosurgery. *Acta Neurochir (Wein)* 1995;63(Suppl):40–3.